



Givlaari™ (givosiran) (Subcutaneous)

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I. Length of Authorization

Coverage will be provided for 6 months initially and may be renewed annually thereafter.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Givlaari 189 mg/mL in a single-dose vial for injection: 2 vials every month

B. Max Units (per dose and over time) [HCPS Unit]:

- 576 billable units every month

III. Initial Approval Criteria^{1,2,3}

Coverage is provided in the following conditions:

Acute hepatic porphyria (AHP) †

- Patient must be 18 years or older; **AND**
- Patient has a definitive diagnosis of acute hepatic porphyria* (including acute intermittent porphyria, variegate porphyria, hereditary coproporphyrin, or ALA dehydratase deficient porphyria) as evidenced by one of the following:
 - Patient has had elevated urinary or plasma PBG (porphobilinogen) and ALA (delta-aminolevulinic acid) levels within the previous year; **OR**
 - Patient has a mutation in an affected gene as identified on molecular genetic testing; **AND**
- Patient has a history of at least two documented porphyria attacks (i.e., requirement of hospitalization, urgent healthcare visit or intravenous administration of hemin) **OR** one severe attack with CNS involvement (e.g., hallucinations, seizures, etc.) during the previous six months; **AND**
- Patient will avoid concomitant use with, or use decreased doses of, CYP1A2 or CYP2D6 substrates, for which minimal concentration changes may lead to serious or life-threatening

toxicities (e.g., clozapine, amitriptyline, theophylline, verapamil, clomipramine, clonidine, etc.); **AND**

- Patient will avoid known triggers of porphyria attacks (i.e., alcohol, smoking, exogenous hormones, hypocaloric diet/fasting, certain medications such as barbiturates, hydantoins, sulfa-antibiotics, anti-epileptics, etc.); **AND**
- Patients currently receiving prophylactic intravenous hemin therapy will discontinue hemin within 3 to 6 months of initiation with givosiran; **AND**
- Patient has not had or is anticipating a liver transplant

*Acute Hepatic Porphyria	Urine delta-aminolevulinic acid (ALA)	Urine porphobilinogen (PBG)	Urine porphyrins	Gene
Acute Intermittent Porphyria (AIP)	Elevated	Elevated	Increased uroporphyrin	<i>HMBS</i>
Hereditary Coproporphyria (HCP)	Elevated	Elevated	Increased coproporphyrin	<i>CPOX</i>
Variegate Porphyria (VP)	Elevated	Elevated	Increased coproporphyrin	<i>PPOX</i>
ALA Dehydratase-Deficiency Porphyria (ADP)	Elevated	Normal	Increased coproporphyrin	<i>ALAD</i>

† FDA Approved Indication(s); ‡ Compendium Recommended Indication(s)

IV. Renewal Criteria¹

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: anaphylactic reactions, severe hepatic toxicity, severe renal toxicity, severe injection site reactions, etc.; **AND**
- Disease response as evidenced by a decrease in the frequency of acute porphyria attacks, and/or hospitalizations/urgent care visits, and/or a decrease requirement of hemin intravenous infusions; **AND**
- Patient has a reduction/normalization of biochemical markers (i.e., ALA, PBG) compared to baseline; **AND**
- Patient will not use in combination with prophylactic intravenous hemin therapy; **AND**
- Patient has not received a liver transplant

V. Dosage/Administration

Indication	Dose
Acute Hepatic Porphyria (AHP)	<p>For administration by a healthcare professional as a subcutaneous injection only.</p> <ul style="list-style-type: none"> • Administer 2.5 mg/kg via subcutaneous injection once monthly. Dosing is based on actual body weight.

VI. Billing Code/Availability Information

HCPCS:

- J3490 – Unclassified drugs
- C9399 – Unclassified drugs or biologicals (*Hospital outpatient use only*)
- C9056 – Injection, givosiran, 0.5 mg; 1 billable unit = 0.5 mg (*Effective 04/01/2020 – 06/30/2020*)
- J0223 – Injection, givosiran, 0.5 mg; 1 billable unit=0.5 mg (*Effective 07/01/2020*)
- NDC:
 - Givlaari 189 mg/mL in a single-dose vial for injection: 71336-1001-xx

VII. References

1. Givlaari [package insert]. Cambridge, MA; Alnylam Pharm., Inc., November 2019. Accessed November 2019.
2. Whatley SD, Badminton MN. Acute Intermittent Porphyria. 2005 Sep 27 [Updated 2013 Feb 7]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2019. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1193/>.
3. Anderson KE. Porphyrias: An overview. Mahoney DH, ed. UpToDate. Waltham, MA: UpToDate Inc. https://www.uptodate.com/contents/porphyrias-an-overview?search=acute%20hepatic%20porphyria&source=search_result&selectedTitle=3~91&usage_type=default&display_rank=3 (Accessed on January 02, 2017.).
4. Balwani M, Gouya L, Rees D, et al. GS-14-ENVISION, a phase 3 study to evaluate efficacy and safety of givosiran, an investigational RNAi therapeutic targeting aminolevulinic acid synthase 1, in acute hepatic porphyria patients. *J Hepatology*:Apr2019;Vol70;Iss. 1, Suppl;pps e81–e82

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E80.20	Unspecified porphyria
E80.21	Acute intermittent (hepatic) porphyria
E80.29	Other porphyria

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC